

REMARKS

Applicants submit that the amendment to the claims do not introduce new matter
5 and are fully supported by the specification and claims as originally filed. Applicants
submit that the present claims meet all the requirements for patentability. The Examiner is
respectfully requested to allow all the present claims. If the Examiner is of a contrary
view, the Examiner is requested to contact the undersigned attorney at (215) 557-3861.

10 Attached hereto is a marked-up version of the changes made to the specification
and the claims by the current amendment. The attached page is captioned "VERSION
WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

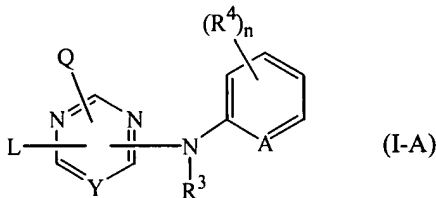
In the claims:

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Please cancel claims 11 and 23, without prejudice.

Please amend claims 1-22 and 24, as follows:

- 10 1. (amended) A particle consisting of a solid dispersion, comprising:
(b) a compound of formula



a N-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof,

15

wherein

Y is CR⁵ or N;

A is CH, CR⁴ or N;

n is 0, 1, 2, 3 or 4;

Q is $\text{-NR}^1\text{R}^2$ or when Y is CR^5 then Q may also be hydrogen;

20

R^1 and R^2 are each independently selected from hydrogen, hydroxy,

C₁₋₁₂alkyl, C₁₋₁₂alkyloxy, C₁₋₁₂alkylcarbonyl, C₁₋₁₂alkyloxycarbonyl, aryl, amino, mono- or di(C₁₋₁₂alkyl)amino, mono- or di(C₁₋₁₂alkyl)aminocarbonyl wherein each of the aforementioned C₁₋₁₂alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, hydroxyC₁₋₆alkyloxy, carboxyl, C₁₋₆alkyloxycarbonyl, cyano, amino, imino, aminocarbonyl, aminocarbonylamino, mono- or di(C₁₋₆alkyl)amino, aryl

25

and Het; or R¹ and R² taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C₁₋₁₂alkyl)aminoC₁₋₄alkylidene;

R³ is hydrogen, aryl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyl substituted with C₁₋₆alkyloxycarbonyl; [and]

each R⁴ independently is hydroxy, halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, or when Y is CR⁵ then R⁴ may also represent C₁₋₆alkyl substituted with cyano or aminocarbonyl;

R⁵ is hydrogen or C₁₋₄alkyl;

L is -X¹-R⁶ or -X²-Alk-R⁷, wherein

R⁶ and R⁷ each independently are phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl, formyl, cyano, nitro, amino, and trifluoromethyl; or when Y is CR⁵ then R⁶ and R⁷ may also be selected from phenyl substituted with one, two, three, four or five substituents each independently selected from aminocarbonyl, trihalomethyloxy and trihalomethyl; or when Y is N then R⁶ and R⁷ may also be selected from indanyl or indolyl, each of said indanyl or indolyl may be substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl, formyl, cyano, nitro, amino, and trifluoromethyl;

X¹ and X² are each independently -NR³-, -NH-NH-, -N=N-, -O-, -S-, -S(=O)- or -S(=O)₂-;

Alk is C₁₋₄alkanediyl; or

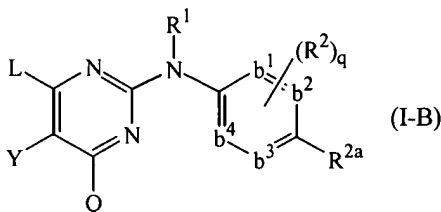
when Y is CR⁵ then L may also be selected from C₁₋₁₀alkyl, C₃₋₁₀alkenyl, C₃₋₁₀alkynyl, C₃₋₇cycloalkyl, or C₁₋₁₀alkyl substituted

with one or two substituents independently selected from C₃₋₇ cycloalkyl, indanyl, indolyl and phenyl, wherein said phenyl, indanyl and indolyl may be substituted with one, two, three, four or where possible five substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, aminocarbonyl, C₁₋₆alkyloxycarbonyl, formyl, nitro, amino, trihalomethyl, trihalomethoxy and C₁₋₆alkylcarbonyl;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C₁₋₆alkyl, C₁₋₆alkyloxy, cyano, nitro and trifluoromethyl;

[or

a compound of formula



the *N*-oxides, the pharmaceutically acceptable addition salts, quaternary amines and the stereochemically isomeric forms thereof, wherein

-b¹=b²-C(R^{2a})=b³-b⁴= represents a bivalent radical of formula

-CH=CH-C(R^{2a})=CH-CH= (b-1);

-N=CH-C(R^{2a})=CH-CH= (b-2);

-CH=N-C(R^{2a})=CH-CH= (b-3);

-N=CH-C(R^{2a})=N-CH= (b-4);

-N=CH-C(R^{2a})=CH-N= (b-5);

-CH=N-C(R^{2a})=N-CH= (b-6);

-N=N-C(R^{2a})=CH-CH= (b-7);

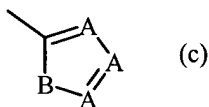
q is 0, 1, 2; or where possible q is 3 or 4;

R¹ is hydrogen, aryl, formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyl substituted with formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl;

R^{2a} is cyano, aminocarbonyl, mono- or di(methyl)aminocarbonyl, C_{1-6} alkyl substituted with cyano, aminocarbonyl or mono- or di(methyl)aminocarbonyl, C_{2-6} alkenyl substituted with cyano, or C_{2-6} alkynyl substituted with cyano;

each R^2 independently is hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or

- 5 $-C(=O)R^6$, C_{3-7} cycloalkyl, C_{2-6} alkenyl optionally substituted with one or more halogen atoms or cyano, C_{2-6} alkynyl optionally substituted with one or more halogen atoms or cyano, C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, $-S(=O)_pR^6$, $-NH-S(=O)_pR^6$, $-C(=O)R^6$, $-NHC(=O)H$, $-C(=O)NHNH_2$, $-NHC(=O)R^6$, $-C(=NH)R^6$ or a radical of formula



wherein each A independently is N, CH or CR^6 ;

B is NH, O, S or NR^6 ;

p is 1 or 2; and

- 15 R^6 is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-7} cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

- * C_{3-7} cycloalkyl,
 - * indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C_{1-6} alkyl, hydroxy, C_{1-6} alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C_{1-6} alkylcarbonyl,
 - * phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R^2 ; or
- 20 25

L is $-X-R^3$ wherein

R^3 is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R^2 ; and

X is $-NR^1-$, $-NH-NH-$, $-N=N-$, $-O-$, $-C(=O)-$, $-CHOH-$, $-S-$, $-S(=O)-$ or $-S(=O)_2-$;

5 Q represents hydrogen, C_{1-6} alkyl, halo, polyhalo C_{1-6} alkyl or $-NR^4R^5$; and

R^4 and R^5 are each independently selected from hydrogen, hydroxy, C_{1-12} alkyl, C_{1-12} alkyloxy, C_{1-12} alkylcarbonyl, C_{1-12} alkyloxycarbonyl, aryl, amino, mono- or di(C_{1-12} alkyl)amino, mono- or di(C_{1-12} alkyl)aminocarbonyl wherein each of the
10 aforementioned C_{1-12} alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C_{1-6} alkyloxy, hydroxy C_{1-6} alkyloxy, carboxyl, C_{1-6} alkyloxycarbonyl, cyano, amino, imino, mono- or di(C_{1-6} alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, $-S(=O)_pR^6$, $-NH-S(=O)_pR^6$, $-C(=O)R^6$, $-NHC(=O)H$, $-C(=O)NHNH_2$, $-NHC(=O)R^6$, $-C(=NH)R^6$, aryl and Het; or

15 R^4 and R^5 taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C_{1-12} alkyl)amino C_{1-4} alkylidene;

Y represents hydroxy, halo, C_{3-7} cycloalkyl, C_{2-6} alkenyl optionally substituted with one or more halogen atoms, C_{2-6} alkynyl optionally substituted with one or more halogen atoms, C_{1-6} alkyl substituted with cyano or $-C(=O)R^6$, C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, $-S(=O)_pR^6$, $-NH-S(=O)_pR^6$, $-C(=O)R^6$, $-NHC(=O)H$, $-C(=O)NHNH_2$, $-NHC(=O)R^6$, $-C(=NH)R^6$ or aryl;

20 aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{1-6} alkyloxy, cyano, nitro, polyhalo C_{1-6} alkyl and polyhalo C_{1-6} alkyloxy;

25 Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic heterocyclic

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(a-1);

(a-2);

(a-3);

(a-4);

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(a-5);

n is 0, 1, 2, 3 or 4; and in case $-a^1=a^2-a^3=a^4-$ is $(a-1)$, then n may also be 5;

R¹ is hydrogen, aryl, formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyl substituted with formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl; and

each R² independently is hydroxy, halo, C₁₋₆alkyl optionally substituted with cyano or

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$$-\text{S}(=\text{O})_p\text{R}^4, \quad -\text{NH}-\text{S}(=\text{O})_p\text{R}^4, \quad -\text{C}(=\text{O})\text{R}^4, \quad -\text{NHC}(=\text{O})\text{H}, \quad -\text{C}(=\text{O})\text{NHNH}_2,$$

25



wherein each A independently is N, CH or CR⁴;

B is NH, O, S or NR⁴;

p is 1 or 2; and

R⁴ is methyl, amino, mono- or dimethylamino or polyhalomethyl;

- 5 L is C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₇cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

* C₃₋₇cycloalkyl,

- 10 * indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C₁₋₆alkylcarbonyl,

* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; or

- 15 L is -X-R³ wherein

R³ is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; and

X is -NR¹-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)₂-;

- 20 aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C₁₋₆alkyl, C₃₋₇cycloalkyl, C₁₋₆alkyloxy, cyano, nitro, polyhaloC₁₋₆alkyl and polyhaloC₁₋₆alkyloxy;

with the proviso that compounds wherein

- * L is C₁₋₃alkyl; R¹ is selected from hydrogen, ethyl and methyl; -a¹=a²-a³=a⁴-
25 represents a bivalent radical of formula (a-1); n is 0 or 1 and R² is selected from fluoro, chloro, methyl, trifluoromethyl, ethyloxy and nitro; or
- * L is -X-R³, X is -NH-; R¹ is hydrogen; -a¹=a²-a³=a⁴- represents a bivalent radical of formula (a-1); n is 0 or 1 and R² is selected from chloro, methyl, methyloxy, cyano,

amino and nitro and R³ is phenyl, optionally substituted with one substituent selected from chloro, methyl, methyloxy, cyano, amino and nitro;

and the compounds

- * *N,N'*-dipyridinyl-(1,3,5)-triazine-2,4-diamine;
 - 5 * (4-chloro-phenyl)-(4(1-(4-isobutyl-phenyl)-ethyl)-(1,3,5) triazin-2-yl)-amine
- are not included;] and

(b) one or more pharmaceutically acceptable water-soluble polymers.

10 2. (amended) A particle according to claim 1, 25 or 26 having a particle size of less than 1500 μm .

3. (amended) A particle according to claim 1, 25 or 26, [or 2] wherein [the] said compound (a) [of formula (I-A), (I-B) or (I-C)] is in a non-crystalline phase.

15 4. (amended) A particle according to claim [3] 1, 25 or 26, wherein the solid dispersion is in the form of a solid solution comprising said compound (a) and said polymer (b). [, or in the form of a dispersion wherein amorphous or microcrystalline (a) or amorphous or microcrystalline (b) is dispersed more or less evenly in a solid solution comprising said (a) and said (b)].

20 5. (amended) A particle consisting of a solid dispersion, comprising:

(a) a compound selected from the group consisting of

[according to the preceding claims wherein the compound of formula (I-A), (I-B) or (I-C) is] 4-[[4-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile 4-[[4-amino-5-bromo-6-(4-cyano-2,6-dimethylphenoxy)-2-pyrimidinyl]amino]benzonitrile [(R165335)], 4-[[4-amino-5-chloro-6-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]amino]-benzonitrile [(], 4-[[5-chloro-4-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile, (4-[[5-bromo-4-(4-cyano-2,6-dimethylphenoxy)-2-pyrimidinyl]amino]benzonitrile, (4-[[4-amino-5-

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chloro-6-[(4-cyano-2,6-dimethylphenyl)amino]-2-pyrimidinyl]amino]-
benzonitrile, (4-[[5-bromo-6-[(4-cyano-2,6-dimethylphenyl)amino]-2-
pyrimidinyl]amino]benzonitrile, (4-[[4-amino-5-chloro-6-(4-cyano-2,6-
dimethylphenoxy)-2-pyrimidinyl]amino]benzonitrile, (4-[[2-
5
[(cyanophenyl)amino]-4-pyrimidinyl]amino]-3,5-dimethylbenzonitrile, [(
or] and 4-[[4-[(2,4,6-trimethylphenyl)amino]-1,3,5-triazin-2-
yl]amino]benzonitrile; and

(b) one or more pharmaceutically acceptable water-soluble polymers.

10 6. (amended) A particle according to [the preceding claims] claim 1, wherein [the
compound of formula (I-A)] said compound (a) is 4-[[4-[(2,4,6-
trimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile.

15 7. (amended) A particle according to [the preceding claims] claim 1, 25 or 26, wherein
[the] said water-soluble polymer is a polymer that has an apparent viscosity of 1 to
5000 mPa·s when dissolved at 20°C in an aqueous solution at 2% (w/v).

8. (amended) A particle according to claim 7, wherein the water-soluble polymer is a
polymer selected from the group [comprising] consisting of:

20 [-] alkylcelluloses [such as methylcellulose],

[-] hydroxyalkylcelluloses [such as hydroxymethylcellulose, hydroxyethylcellulose,
hydroxypropylcellulose and hydroxybutylcellulose],

[-] hydroxyalkyl alkylcelluloses [such as hydroxyethyl methylcellulose and
hydroxypropyl methylcellulose],

25 [-] carboxyalkylcelluloses [such as carboxymethylcellulose],

[-] alkali metal salts of carboxyalkylcelluloses [such as sodium carboxymethyl-
cellulose],

[-] carboxyalkylalkylcelluloses [such as carboxymethylethylcellulose],

[-] carboxyalkylcellulose esters,

[-]starches,

[-] pectines [such as sodium carboxymethylamylopectine],

[-] chitin derivatives [derivates such as chitosan],

5 [-] di-, oligo- or polysaccharides [such as trehalose, cyclodextrins or a derivative thereof, alginic acid, alkali metal and ammonium salts thereof, carrageenans, galactomannans, tragacanth, agar-agar, gummi arabicum, guar gummi and xanthan gummi],

[-] polyacrylic acids and the salts thereof,

[-] polymethacrylic acids, the salts and esters thereof, methacrylate copolymers,

10 [-]polyvinylalcohol, and

[-]polyalkylene oxides [such as polyethylene oxide and polypropylene oxide and copolymers of ethylene oxide and propylene oxide].

15 9. (amended) A particle according to claim 8, wherein [the] said water-soluble polymer is hydroxypropyl methylcellulose [HPMC 29105 mPa·s].

10. (amended) A particle according to claim 9, wherein the [weight-by-]weight ratio of (a):(b) is in the range of 1:1 to 1:899.

20 11. CANCELLED

12. (amended) A particle according to [any one of the preceding claims] claim 1, 25 or 26 consisting of a solid solution, comprising:

25 (a) two parts by weight of [a compound of formula (I-A), (I-B) or (I-C)] said compound (a); and

(b) three parts by weight of hydroxypropyl methylcellulose [HPMC 2910 5 mPa·s, obtainable by blending said components, extruding the blend at a temperature in the range of 20°C-300°C, grinding the extrudate, and optionally sieving the obtained particles].

13. (amended) A particle according to [any one of the preceding claims] claim 1, 25 or 26, further comprising one or more pharmaceutically acceptable excipients.

5 14. (amended) A pharmaceutical dosage form, comprising a therapeutically effective amount of particles as claimed in [any one of the preceding claims] claim 1, 25 or 26.

10 15. (amended) A pharmaceutical dosage form according to claim 14 [adapted for oral administration], wherein said form is shaped as a tablet suitable for oral administration.

15 16. (amended) A pharmaceutical dosage form according to claim 15, [for immediate release of a compound of formula (I-A), (I-B) or (I-C) upon oral ingestion] wherein said particles are homogeneously distributed throughout a mixture of a diluent and a disintegrant for immediate release of said compound.

20 17. (amended) A pharmaceutical dosage form according to claim 15 [or 16], wherein said tablet is surrounded by a film-coat comprising a film-forming polymer, a plasticizer and optionally a pigment.

25 18. (amended) A pharmaceutical dosage form according to claim 16,
wherein [the] said diluent is a spray-dried mixture [of] comprising:
(a) 25% by weight of lactose monohydrate; and
(b) 75% by weight of microcrystalline cellulose [(75:25)]; [and]
wherein [the] said disintegrant is selected from the group consisting of
crospovidone [or] and croscarmellose.

30 19. (amended) A pharmaceutical dosage form according to [any one of claims 14 to 18] claim 14, wherein [the weight of said particles] said therapeutically effective

amount is at least 40 % of the total weight of [the] said pharmaceutical dosage form.

20. (amended) A process of preparing particles as claimed in [any one of claims 1 to 13]
5 claim 1, 25 or 26, comprising the steps of: [characterized by]

(1) blending [the components,] said compound (a) and said polymer (b) to form a blend;

(2) extruding said blend at a temperature in the range of 20-300°C to form an extrudate[.];

10 (3) grinding [the] said extrudate to form particles[.]; and

(4) optionally, sieving [the] said particles.

21. (amended) A process of preparing a pharmaceutical dosage form as claimed in [any one of claims 14 to 18] claim 14, comprising the steps of: [characterized by]

15 (1) blending [a] said therapeutically effective amount of particles [as claimed in any one of claims 1 to 13] with pharmaceutically acceptable excipients; and

(2) compressing said blend into tablets [or filling said blend in capsules].

22. (amended) A method of treating a mammal suffering from a viral infection, comprising the steps of:

20 (1) [Particles according to any one of claims 1 to 13 for use in] preparing a pharmaceutical dosage form of said particles according to claim 1, 25 or 26;

25 (2) administering [,for oral administration to a mammal suffering from a viral infection, wherein] a single dose of said pharmaceutical dosage form [such dosage form can be administered] once daily to said mammal.

23. CANCELLED

30 24. A pharmaceutical package suitable for commercial sale, comprising:

(a) a container[,];

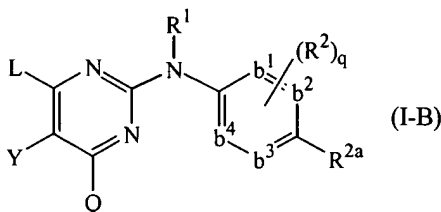
(b) written matter on said container;

(c) [an oral] said pharmaceutical dosage form [of a compound of formula (I-A), (I-B) or (I-C)] as claimed in [any one of claims 14 to 19, and] claim 14;
 5 wherein said [associated with said package] written matter is associated
with said pharmaceutical dosage form.

Please add the following new claims:

10 25. A particle consisting of a solid dispersion, comprising:

(a) a compound of formula



the *N*-oxides, the pharmaceutically acceptable addition salts, quaternary amines and the stereochemically isomeric forms thereof,

15 wherein

-b¹=b²-C(R^{2a})=b³-b⁴= represents a bivalent radical of formula

-CH=CH-C(R^{2a})=CH-CH= (b-1);

-N=CH-C(R^{2a})=CH-CH= (b-2);

-CH=N-C(R^{2a})=CH-CH= (b-3);

20 -N=CH-C(R^{2a})=N-CH= (b-4);

-N=CH-C(R^{2a})=CH-N= (b-5);

-CH=N-C(R^{2a})=N-CH= (b-6);

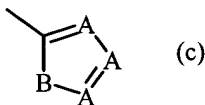
-N=N-C(R^{2a})=CH-CH= (b-7);

q is 0, 1, 2; or where possible q may also be 3 or 4;

R^1 is hydrogen, aryl, formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkyl substituted with formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl;

R^{2a} is cyano, aminocarbonyl, mono- or di(methyl)aminocarbonyl, C_{1-6} alkyl substituted with cyano, aminocarbonyl or mono- or di(methyl)aminocarbonyl, C_{2-6} alkenyl substituted with cyano, or C_{2-6} alkynyl substituted with cyano;

each R^2 independently is hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or $-C(=O)R^6$, C_{3-7} cycloalkyl, C_{2-6} alkenyl optionally substituted with one or more halogen atoms or cyano, C_{2-6} alkynyl optionally substituted with one or more halogen atoms or cyano, C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, $-S(=O)_pR^6$, $-NH-S(=O)_pR^6$, $-C(=O)R^6$, $-NHC(=O)H$, $-C(=O)NHNH_2$, $-NHC(=O)R^6$, $-C(=NH)R^6$ or a radical of formula



wherein

each A independently is N, CH or CR^6 ;

B is NH, O, S or NR^6 ;

p is 1 or 2; and

R^6 is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-7} cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

C_{3-7} cycloalkyl,

indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C_{1-6} alkyl, hydroxy, C_{1-6} alkyloxy, cyano, aminocarbonyl,

nitro, amino, polyhalomethyl, polyhalomethoxy and C₁₋₆alkylcarbonyl,

phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; or

L is -X-R³ wherein

R³ is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; and

X is -NR¹-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH, -S-, -S(=O)- or -S(=O)₂-;

Q is hydrogen, C₁₋₆alkyl, halo, polyhaloC₁₋₆alkyl or -NR⁴R⁵; and

R⁴ and R⁵ are each independently selected from hydrogen, hydroxy, C₁₋₁₂alkyl, C₁₋₁₂alkyloxy, C₁₋₁₂alkylcarbonyl, C₁₋₁₂alkyloxycarbonyl, aryl, amino, mono- or di(C₁₋₁₂alkyl)amino, mono- or di(C₁₋₁₂alkyl)aminocarbonyl wherein each of the aforementioned C₁₋₁₂alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, hydroxyC₁₋₆alkyloxy, carboxyl, C₁₋₆alkyloxycarbonyl, cyano, amino, imino, mono- or di(C₁₋₆alkyl)amino, polyhalomethyl, polyhalomethoxy, polyhalomethylthio, -S(=O)_pR⁶, -NH-S(=O)_pR⁶, -C(=O)R⁶, -NHC(=O)H, -C(=O)NHNH₂, -NHC(=O)R⁶, -C(=NH)R⁶, aryl and Het; or

R⁴ and R⁵ taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C₁₋₁₂alkyl)aminoC₁₋₄alkylidene;

Y represents hydroxy, halo, C₃₋₇cycloalkyl, C₂₋₆alkenyl optionally substituted with one or more halogen atoms, C₂₋₆alkynyl optionally

substituted with one or more halogen atoms, C₁₋₆alkyl substituted with cyano or -C(=O)R⁶, C₁₋₆alkyloxy, C₁₋₆alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C₁₋₆alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)_pR⁶, -NH-S(=O)_pR⁶,
 5 -C(=O)R⁶, -NHC(=O)H, -C(=O)NHNH₂, -NHC(=O)R⁶, -C(=NH)R⁶ or aryl;

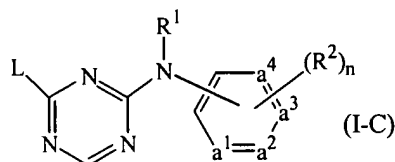
aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C₁₋₆alkyl, C₃₋₇ cycloalkyl, C₁₋₆alkyloxy, cyano, nitro, polyhaloC₁₋₆ alkyl and polyhaloC₁₋₆alkyloxy;

10 Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl wherein each of said aliphatic heterocyclic radical may optionally be substituted with an
 15 oxo group; and said aromatic heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy; and

(b) one or more pharmaceutically acceptable water-soluble polymers.

20 26. A particle consisting of a solid dispersion, comprising

(a) a compound of formula



25 the *N*-oxides, the pharmaceutically acceptable addition salts, quaternary amines and the stereochemically isomeric forms thereof,

wherein

$-a^1=a^2-a^3=a^4-$ represents a bivalent radical of formula

$-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ (a-1);

$-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ (a-2);

5 $-\text{N}=\text{CH}-\text{N}=\text{CH}-$ (a-3);

$-\text{N}=\text{CH}-\text{CH}=\text{N}-$ (a-4);

$-\text{N}=\text{N}-\text{CH}=\text{CH}-$ (a-5);

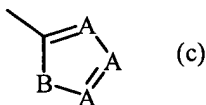
n is 0, 1, 2, 3 or 4; and in case $-a^1=a^2-a^3=a^4-$ is (a-1), then n may also be 5;

10 R^1 is hydrogen, aryl, formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkyl substituted with formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl;

each R^2 independently is hydroxy, halo, C_{1-6} alkyl optionally substituted with cyano or $-\text{C}(=\text{O})\text{R}^4$, C_{3-7} cycloalkyl, C_{2-6} alkenyl optionally substituted with one or more halogen atoms or cyano, C_{2-6} alkynyl optionally substituted with one or more halogen atoms or cyano, C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C_{1-6} alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, $-\text{S}(=\text{O})_p\text{R}^4$, $-\text{NH}-\text{S}(=\text{O})_p\text{R}^4$, $-\text{C}(=\text{O})\text{R}^4$, $-\text{NHC}(=\text{O})\text{H}$, $-\text{C}(=\text{O})\text{NHNH}_2$, $-\text{NHC}(=\text{O})\text{R}^4$, $-\text{C}(=\text{NH})\text{R}^4$ or a radical of formula

15

20



wherein

each A independently is N, CH or CR^4 ;

B is NH, O, S or NR^4 ;

25 p is 1 or 2; and

R^4 is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₃₋₇cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

C₃₋₇cycloalkyl;

indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C₁₋₆alkylcarbonyl,

phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; or

L is -X-R³ wherein

R³ is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R²; and

X is -NR¹-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)₂-;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C₁₋₆alkyl, C₃₋₇cycloalkyl, C₁₋₆alkyloxy, cyano, nitro, polyhaloC₁₋₆alkyl and polyhaloC₁₋₆alkyloxy;

with the proviso that compounds wherein

- (i) L is C₁₋₃alkyl; R¹ is selected from hydrogen, ethyl and methyl; -a¹=a²-a³=a⁴- represents a bivalent radical of formula (a-1); n is 0 or 1 and R² is selected from fluoro, chloro, methyl, trifluoromethyl, ethyloxy and nitro;
- (ii) L is -X-R³, X is -NH-; R¹ is hydrogen; -a¹=a²-a³=a⁴- represents a bivalent radical of formula (a-1); n is 0 or 1 and R² is selected from

chloro, methyl, methyloxy, cyano, amino and nitro and R^3 is phenyl, optionally substituted with one substituent selected from chloro, methyl, methyloxy, cyano, amino and nitro;

(iii) *N,N'*-dipyridinyl-(1,3,5)-triazine-2,4-diamine; and

(iv) (4-chloro-phenyl)-(4(1-(4-isobutyl-phenyl)-ethyl)-(1,3,5)triazin-2-yl)-amine

are not included; and

(b) one or more pharmaceutically acceptable water-soluble polymers.

27. A process of preparing a pharmaceutical dosage form as claimed in claim 14, comprising the steps of:

(a) blending a therapeutically effective amount of particles with pharmaceutically acceptable excipients to form a blend; and

(b) filling said blend into capsules.

28. A particle according to claim 4, further comprising a material selected from said compound (a) and said polymer (b);

wherein said material is dispersed in said solid solution to form a solid dispersion;

wherein said compound (a) is in a form selected from amorphous and microcrystalline; and

wherein said polymer (b) is in a form selected from amorphous and microcrystalline.

29. A particle produced by the process of claim 20.